IGF2 gene

insulin like growth factor 2

Normal Function

The *IGF2* gene provides instructions for making a protein called insulin-like growth factor 2. This protein plays an essential role in growth and development before birth. Studies suggest that insulin-like growth factor 2 promotes the growth and division (proliferation) of cells in many different tissues. Although the *IGF2* gene is highly active during fetal development, it is much less active after birth.

People inherit one copy of most genes from their mother and one copy from their father. Both copies are typically active, or "turned on," in cells. However, the activity of the *IGF2* gene depends on which parent it was inherited from. In most tissues, only the copy inherited from a person's father (the paternally inherited copy) is active; the copy inherited from the mother (the maternally inherited copy) is not active. This sort of parent-specific difference in gene activation is caused by a phenomenon called genomic imprinting.

IGF2 is part of a cluster of genes on the short (p) arm of chromosome 11 that undergo genomic imprinting. Another gene in this cluster, *H19*, is also involved in growth and development. A nearby region of DNA known as imprinting center 1 (IC1) or the H19 differentially methylated region (H19 DMR) controls the parent-specific genomic imprinting of both the *IGF2* and *H19* genes. The IC1 region undergoes a process called methylation, which is a chemical reaction that attaches small molecules called methyl groups to certain segments of DNA. Methylation, which occurs during the formation of an egg or sperm cell, is a way of marking or "stamping" the parent of origin. The IC1 region is normally methylated only on the paternally inherited copy of chromosome 11.

Health Conditions Related to Genetic Changes

Beckwith-Wiedemann syndrome

Beckwith-Wiedemann syndrome, a condition characterized by overgrowth and other signs and symptoms that affect many parts of the body, can result from changes that affect the IC1 region. In some people with this condition, both the maternally inherited copy and the paternally inherited copy of the IC1 region have methyl groups attached (hypermethylation). Because the IC1 region controls the genomic imprinting of the *IGF2* and *H19* genes, this abnormality disrupts the regulation of both genes. Specifically, hypermethylation of the IC1 region leads to increased activity of the *IGF2* gene and a loss of *H19* gene activity in many tissues. An increase in *IGF2* gene activity, which promotes growth, and a loss of *H19* gene activity, which normally

restrains growth, together lead to overgrowth in people with Beckwith-Wiedemann syndrome.

In a few cases, Beckwith-Wiedemann syndrome has been caused by deletions of a small amount of DNA from the IC1 region. Like abnormal methylation, these deletions alter the activity of the *IGF2* and *H19* genes.

prostate cancer

Russell-Silver syndrome

Changes in methylation of the IC1 region are also responsible for some cases of Russell-Silver syndrome, a disorder characterized by slow growth before and after birth. The changes are different than those seen in Beckwith-Wiedemann syndrome and have the opposite effect on growth.

In Russell-Silver syndrome, the paternally inherited copy of the IC1 region often has too few methyl groups attached (hypomethylation). Hypomethylation of the IC1 region leads to a loss of *IGF2* gene activity and increased activity of the *H19* gene in many tissues. A loss of *IGF2* gene activity, which normally promotes growth, and an increase in *H19* gene activity, which restrains growth, together lead to poor growth and short stature in people with Russell-Silver syndrome.

cancers

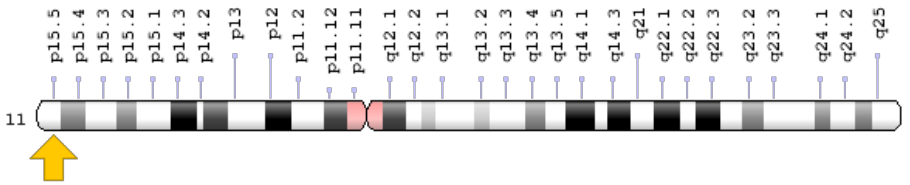
Increased activity of the *IGF2* gene has been associated with many types of cancer. Normally, the *IGF2* gene undergoes genomic imprinting and only the copy inherited from a person's father is active. In some cancers, however, both the paternally inherited and the maternally inherited copies of the gene are active, increasing the amount of insulin-like growth factor 2 that cells can produce. This phenomenon is known as loss of imprinting (LOI). An increased amount of insulin-like growth factor 2 may stimulate the growth of tumor cells and prevent damaged cells from being destroyed.

Loss of imprinting of the *IGF2* gene has been identified in several types of cancer known as embryonal tumors. These tumors include a form of kidney cancer called Wilms tumor, a cancer of muscle tissue called rhabdomyosarcoma, and a form of liver cancer called hepatoblastoma. Loss of imprinting of the *IGF2* gene has also been found in many other types of cancer, including cancer of blood-forming cells (leukemia) and cancers of the breast, prostate, lung, colon, and liver. In some types of cancer, increased levels of insulin-like growth factor 2 are associated with tumor progression and a poor prognosis.

Chromosomal Location

Cytogenetic Location: 11p15.5, which is the short (p) arm of chromosome 11 at position 15.5

Molecular Location: base pairs 2,129,112 to 2,149,603 on chromosome 11 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- C11orf43
- FLJ22066
- FLJ44734
- IGF-2
- IGF-II
- IGF2_HUMAN
- INSIGF
- insulin-like growth factor 2
- insulin-like growth factor 2 (somatomedin A)
- insulin-like growth factor II
- insulin-like growth factor type 2
- pp9974
- putative insulin-like growth factor II associated protein
- somatomedin A

Additional Information & Resources

Educational Resources

- The Cell: A Molecular Approach (second edition, 2000): DNA Methylation https://www.ncbi.nlm.nih.gov/books/NBK9904/#A1014

GeneReviews

- Beckwith-Wiedemann Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1394
- Russell-Silver Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1324

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28IGF2%5BTIAB%5D%29+OR+%28insulin-like+growth+factor+2%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+360+days%22%5Bdp%5D

OMIM

- H19/IGF2-IMPRINTING CONTROL REGION
  http://omim.org/entry/616186
- INSULIN-LIKE GROWTH FACTOR II
  http://omim.org/entry/147470

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_IGF2.html
- Cancer Genetics Web
  http://www.cancerindex.org/geneweb/IGF2.htm
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=IGF2%5Bgene%5D
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=5466
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/3481
- UniProt
  http://www.uniprot.org/uniprot/P01344

Sources for This Summary

- Abu-Amero S, Monk D, Frost J, Preece M, Stanier P, Moore GE. The genetic aetiology of Silver-Russell syndrome. J Med Genet. 2008 Apr;45(4):193-9. Epub 2007 Dec 21. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18156438
- Bergman D, Halje M, Nordin M, Engström W. Insulin-like growth factor 2 in development and disease: a mini-review. Gerontology. 2013;59(3):240-9. doi: 10.1159/000343995. Epub 2012 Dec 20. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23257688
- Cerrato F, Sparago A, Verde G, De Crescenzo A, Citro V, Cubellis MV, Rinaldi MM, Boccuto L, Neri G, Magnani C, D'Angelo P, Collini P, Perotti D, Sebastio G, Maher ER, Riccio A. Different mechanisms cause imprinting defects at the IGF2/H19 locus in Beckwith-Wiedemann syndrome and Wilms' tumour. Hum Mol Genet. 2008 May 15;17(10):1427-35. doi: 10.1093/hmg/ddn031. Epub 2008 Feb 1.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18245780
- Eggermann T. Silver-Russell and Beckwith-Wiedemann syndromes: opposite (epi)mutations in 11p15 result in opposite clinical pictures. Horm Res. 2009 Apr;71 Suppl 2:30-5. doi: 10.1159/000192433. Epub 2009 Apr 29. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19407494
- Kaneda A, Wang CJ, Cheong R, Timp W, Onyango P, Wen B, Iacobuzio-Donahue CA, Ohlsson R, Andraos R, Pearson MA, Sharov AA, Longo DL, Ko MS, Levchenko A, Feinberg AP. Enhanced sensitivity to IGF-II signaling links loss of imprinting of IGF2 to increased cell proliferation and tumor risk. Proc Natl Acad Sci U S A. 2007 Dec 26;104(52):20926-31. Epub 2007 Dec 17.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18087038
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2409243/
- Livingstone C. IGF2 and cancer. Endocr Relat Cancer. 2013 Oct 24;20(6):R321-39. doi: 10.1530/ERC-13-0231. Print 2013 Dec. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/24080445
- Pickard A, McCance DJ. IGF-Binding Protein 2 - Oncogene or Tumor Suppressor? Front Endocrinol (Lausanne). 2015 Feb 27;6:25. doi: 10.3389/fendo.2015.00025. eCollection 2015. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/25774149
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4343188/
- Sparago A, Cerrato F, Vernucci M, Ferrero GB, Silengo MC, Riccio A. Microdeletions in the human H19 DMR result in loss of IGF2 imprinting and Beckwith-Wiedemann syndrome. Nat Genet. 2004 Sep;36(9):958-60. Epub 2004 Aug 15.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15314640

Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/gene/IGF2

Reviewed: June 2015
Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services